

REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 1-4, 6, 8, 10-16, 19-21, 23-24, and 26-138 will be pending in this application and presented for examination. Claims 1-4, 6, 8, 10-16, 19-21 and 23-24 have been amended. Claims 9 and 17 have been canceled without prejudice and are rewritten as new claims 26-29. Claims 26-138 are newly added. No new matter has been introduced with the foregoing amendments and newly added claims. Reconsideration is respectfully requested.

I. FORMALITIES

With entry of the present amendment, independent claims 1 and 21 have been amended to recite the transition phrase --consisting essentially of-- in lieu of "comprising." Under MPEP § 2111.03, these claims now embody the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976). In addition, the newly added independent claims 30, 45, 66, 89 and 112 also recite --consisting essentially of-- as the transition phrase.

Claims 1 and 21, as well as their dependent claims, have been amended to delete the term "homogeneous." As explained in detail in section VII below, it is Applicants' position that in view of the transition phrase "consisting essentially of," there is no need to include the term "homogeneous." Support for the amendment to claims 1 and 21 is found, for example, in claim 1 as filed. Further amendments to claims 1 and 21 were made to substitute the American English spelling for "solubilise" and "sulphuric." Claims 8, 10, 11, 12, 14, 20 and 24 have been further amended to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention. These minor amendments were made in an effort to more distinctly claim the subject matter and to expedite prosecution. Support for these amendments is found in the claims themselves, or with regard to the amendment to claim 12, at page 4, lines 2-3. Newly added claims 26-29 recite the same subject matter as canceled claims 9 and 17. No new matter has been introduced with the foregoing amendments and newly added claims..

Claims 26-138 are newly added. New independent claims 30, 45, 66, 89 and 112 are drawn to independent embodiments of a foam, a gel, a lotion, a solution and a final product form, respectively. Again, each independent claim recites the transition phrase of "*consisting essentially of*" and is completely supported by the specification as filed.

New *independent* claims 30, 45, 66, 89 and 112 find support in claim 1 as filed. In addition, on page 4, lines 11-14 of the specification, the final form of the formulation can be *inter alia*, a foam, a gel, a lotion or a solution. These formulations are also supported by the detailed Example section of the specification. More specifically, independent claim 30, which is drawn to a foam or mousse, is illustrated in Example 2; the terms "a higher alcohol" and "stabilizer" are set forth on page 5, lines 26-27 and page 4, line 15, respectively, and exemplified by the terms "cetyl alcohol or stearyl alcohol" and "Polysorbate 60" (*see*, claims 37 and 38) in Example 2 on page 8; the term "antioxidant" is set forth on page 5, line 27. Independent claim 45 is drawn to a gel, and is described at page 4, lines 11-22; and further described at page 12, line 11, through page 13, line 1. Independent claim 66 is drawn to a lotion, and is described in Examples 1, 3, 5-6, and 8-11; the term "stabilizer" is set forth on page 4, line 15; and the term "oil component" is set forth on page 5, line 25. Independent claim 89 is drawn to a solution, and is described in Examples 4, and 7. Further, independent claim 112 is drawn to a final product form in a Markush group with "a penetration agent," and finds support in claim 1 as originally filed; on page 4, lines 11-14; and at the bottom of page 4, line 30, bridging to page 5, lines 1-8. Dependent claims 113-117 are also supported at page 5, lines 1-8.

The new *dependent* claims substantially correspond to the dependent claims already on file, but are drawn to the formulation of their corresponding independent claim. Support for the new *dependent* claims can be found as follows:

Claim	New Claim(s)
1	31
2	48, 67, 90, 118
3	49, 68, 91, 119
4	50, 69, 92, 120
6	51, 70, 93, 121
8	36, 52, 71-72, 94, 95, 96, 122-124
9, 17	26-29, 40-43, 53-56, 73-76, 97-100, 125- 128
10	57, 77, 101, 129
11	58, 78, 102, 130
12	59, 79, 103, 131
13	60, 80, 104, 132
14	32-35, 61, 81-82, 105-106, 133-134
15	62, 83, 107, 135
16	63, 84, 108, 136
19	64, 85, 109, 137
21	44, 65, 88, 111, 138

Further, claims 37-39 find support, for example in Example 2 and page 4, line 25 (homogeneous). Claims 46-47 find support, for example at page 4, lines 20-22. Claim 86 finds support at page 5, lines 25-27. Claims 87, and 110 find support in Examples 1, 3-7 and 8-11. No new matter has been entered with the foregoing amendments and newly added claims. As such, Applicants respectfully request that the amendments and new claims be entered.

II. DOUBLE PATENTING

A. U.S. Patent Application No.10/124,197

The Examiner has rejected claims 1-4, 6, 8-9, 12-18, 21 and 23 under the judicially created doctrine of obviousness-type double patenting for allegedly being obvious over the claims of co-pending U.S. Patent Application No.10/124,197 (now U.S. Patent No. 6,946,120). The Examiner has indicated that the double patenting rejection can be overcome by the filing of a Terminal Disclaimer.

In order to expedite prosecution, Applicants file herewith a Terminal Disclaimer to obviate the double patenting rejection. Accordingly, Appellants respectfully request that the Examiner withdraw this rejection.

B. U.S. Patent Application No.10/949,116

The Examiner has rejected claims 1-4, 6, 8-17, 19-21 and 23-24 under the judicially created doctrine of obviousness-type double patenting for allegedly being obvious over the claims of co-pending U.S. Patent Application No.10/949,116. The Examiner has indicated that the double patenting rejection can be overcome by the filing of a Terminal Disclaimer.

In order to expedite prosecution, Applicants file herewith a Terminal Disclaimer to obviate the double patenting rejection. Accordingly, Appellants respectfully request that the Examiner withdraw this rejection.

III. REJECTION UNDER 35 U.S.C. § 103(a) OVER BAZZANO IN VIEW OF WEINER *et al.* OR YU *et al.*

The Examiner has rejected claims 1-3, 6, 8-9, 12-17, 19, 21, and 23 as allegedly being obvious over Bazzano (U.S. Patent No. 5,183,817) in view of Weiner *et al.* (WO 97/12602) or Yu *et al.* (EP 0 273 202). The Examiner admits that Bazzano does not teach or suggest the use of an acid, but alleges that it would have been obvious to one skilled in the art to modify the formulation of Bazzano to include an acid salt of minoxidil as taught by Weiner *et al.* Alternatively, the Examiner alleges that it would have been obvious to combine the teaching of Bazzano and Yu *et al.*, wherein Yu *et al.* allegedly teach the use of lactic acid. To the extent the

rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

In order to expedite prosecution of the present application, Applicants have followed the Examiner's suggestion and have amended the independent claims to recite -- consisting essentially of-- in lieu of "comprising." These claims now embody the specified components "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention (MPEP § 2111.03).

In view of this amendment, Applicants submit that the claims necessarily exclude the teaching of Bazzano. By its own admission, Bazzano teaches that the addition of a retinoid would materially alter the claimed composition. In fact, Bazzano teaches at column 5, lines 16-29, the following:

The present invention combines the use of retinoid compounds with minoxidil, or its analogs or derivatives or minoxidil-type compounds (hereinafter collectively referred to simply as "minoxidil"). ***The stimulatory actions of both compounds can synergistically promote each others' effect. Retinoids can initiate cell growth and differentiation (not initiated by minoxidil), and minoxidil can promote the vasodilatory and mitogenic action not obtained with the retinoids.*** While neither compound alone may have profound effects on advanced alopecias, in combination the compounds are very effective as promoters of new hair growth in areas of alopecia. [Emphasis added].

Applicants assert that the addition of a retinoid to the present composition would materially alter the claimed composition. From the foregoing it is clear that Bazzano first teaches that the combination of minoxidil and a retinoid is synergistic. As such, it can be appreciated that the combination of agents exhibit greater activity or efficacy than the equivalent concentration of either of the agents alone. Thus, the combination of agents that the Examiner contemplates is a material alteration of the presently claimed composition, as the efficacy of such combination is more than simply additive. Second, Bazzano teaches retinoids can initiate cell growth and differentiation, **not** initiated by minoxidil alone. This function of a retinoid would be a material alteration of the claimed composition and demonstrates that the combination of

minoxidil and a retinoid would necessarily be excluded. Third, Bazzano points out at column 5, lines 30-41 the following:

[t]he net result of application of minoxidil and retinoids is initiation and production of new hair growth and conversion of vellus to terminal hair growth, i.e., the increase in size from a vellus to a terminal hair and the continued and more prolonged maintenance of the hair in the anagen phase. *As noted previously, this effect is obtained not merely as the addition of two compounds, but as synergism, i.e., the combination of these substances in the present invention produces an effect which cannot be produced by either compound separately under conditions of its use and, therefore, represents a major advance in the treatment of alopecia.*

Again, retinoids are necessarily excluded from the presently claimed composition as Bazzano teaches that minoxidil and a retinoid *materially affect* the basic and novel characteristic(s) of either agent alone. "[T]he combination of these substances in the present invention produces an effect which cannot be produced by either compound separately under conditions of its use and, therefore, represents a major advance in the treatment of alopecia." (Please see col. 5, line 37-41).

Without the retinoid compound as part of the Bazzano composition, the composition simply would not work as intended. Under MPEP § 2143.01, in making a *prima facie* case of obviousness, the Examiner's proposed modification *cannot* render the prior art unsatisfactory for its intended purpose:

If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984).

If the intended purpose is destroyed, then the motivation or suggestion to make the proposed modification with the secondary references of Weiner *et al.* or Yu *et al.* no longer exists.

Further, Applicants acknowledge the Examiner's suggestion of including the "consisting essentially of" transition phrase to exclude the retinoid of Bazzano and the lipid

vesicles of Weiner *et al.* In view of the foregoing, Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 103(a) rejection and send this application to issue.

IV. REJECTION UNDER 35 U.S.C. § 103(a) OVER NAVARRO *et al.* IN VIEW OF WEINER *et al.* OR YU *et al.*

Claims 1-4, 6, 8-9, 17, 19, and 21-23 were rejected as allegedly being obvious over Navarro *et al.* (WO 97/03638) in view of Weiner *et al.* or Yu *et al.* The Examiner alleges that Navarro *et al.* teach the use of cyclodextrin to reduce the amount of solvent required to solubilize minoxidil. The Examiner admits that Navarro *et al.* do not teach lactic acid. According to the Examiner Weiner *et al.* teach making materials more hydrophilic to improve penetration through the hair follicles. Apparently, Yu *et al.* is cited for teaching the use of hydroxy acid to enhance the therapeutic effects of pharmaceuticals. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Navarro *et al.* teach encapsulating minoxidil in a cyclodextrin carrier, wherein cyclodextrin functions as a "host" molecule to trap the minoxidil "guest" molecule inside the ring. Navarro *et al.* also teach that the prior art use of solvents such as propylene glycol is to solubilize the active ingredient; however, the use of propylene glycol tends to give a greasy, shiny, and unattractive appearance to the hair upon application. In solving this prior art deficiency, Navarro *et al.* teach the use of cyclodextrin in order to assist in the solubilization of minoxidil while avoiding high amounts of propylene glycol.

Navarro *et al.* states the following:

[t]he amount of γ -cyclodextrin present in the composition for hair is such that it permits a substantial reduction in the amount of solvent for minoxidil which would normally need to be added to achieve a comparable solubility of minoxidil in the absence of the aforementioned cyclodextrin. (Page 3, lines 9-13 of the English translation).

From the foregoing, it is clear that cyclodextrin is an essential element of Navarro *et al.* because it ***must be combined*** with minoxidil in order to impart improved solubility properties to minoxidil, thereby reducing the amount of solvent such as propylene glycol needed

in the formulation. However, the present invention excludes the use of cyclodextrin by virtue of the transition phrase of the claims. As such, the encapsulating technique of Navarro *et al.* is distinguished.

Weiner *et al.* do not supply the deficiencies of Navarro *et al.* Weiner *et al.* teach another encapsulating technology, which is a 2-step process. In particular, Weiner *et al.* teach that minoxidil can be modified to make it more hydrophilic, for example, by converting it to an acid such as a lactic acid salt, or by encapsulating it in cyclodextrin (*see*, page 3, lines 15-19). After the minoxidil has been made more hydrophilic, it *must* thereafter be further encapsulated in a lipid vesicle in order to achieve improved penetration through hair follicles (*see*, page 3, lines 5-10). As such, both Navarro *et al.* and Weiner *et al.* teach the use of encapsulation in order to topically apply minoxidil. Further, Applicants acknowledge the Examiner's suggestion of including the "consisting essentially of" transition phrase to exclude the lipid vesicles of Weiner *et al.* In a similar fashion, the encapsulation of Navarro *et al.* is excluded.

Without either Navarro *et al.* or Weiner *et al.*, Yu *et al.* simply do not teach or suggest the claimed invention. Yu *et al.* do not teach or suggest a composition as recited in any of the independent claims, wherein minoxidil has a concentration of at least 5%, and propylene glycol when present, is less than 10% by weight. In view of the foregoing, Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 103(a) rejection and send this application to issue.

V. REJECTION UNDER 35 U.S.C. § 103(a) OVER BAZZANO IN VIEW OF WEINER *et al.* AND YU *et al.* IN FURTHER VIEW OF CALDINI *et al.*

The Examiner has rejected claims 10-11, 20 and 24 as allegedly being obvious over Bazzano in view of Weiner *et al.* and Yu *et al.* in further view of Caldini *et al.* (U.S. Patent No. 4,272,516). The Examiner alleges that Caldini *et al.* teaches benzyl alcohol having the ability of facilitating the absorption of the other components in the skin and its associated organs. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Bazzano, Weiner *et al.* and Yu *et al.* have been distinguished. Caldini *et al.* do not supply the deficiencies of the primary references. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

VI. REJECTION UNDER 35 U.S.C. § 103(a) OVER NAVARRO *et al.* IN VIEW OF WEINER *et al.* AND YU *et al.* IN FURTHER VIEW OF CALDINI *ET AL.*

The Examiner has rejected claims 10-11, 20 and 24 as allegedly being obvious over Navarro in view of Weiner *et al.* and Yu *et al.* in further view of Caldini *et al.* (U.S. Patent No. 4,272,516). The Examiner alleges that Caldini *et al.* teaches benzyl alcohol having the ability of facilitating the absorption of the other components in the skin and its associated organs. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Navarro, Weiner *et al.* and Yu *et al.* have been distinguished. Caldini *et al.* do not supply the deficiencies of the primary references. Therefore, the claims are not rendered obvious. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

VII. REJECTION UNDER 35 U.S.C. § 103(a) OVER DI SCHIENA (U.S. 4,866,067) IN VIEW OF WEINER *et al.*

The Examiner has rejected claims 1-3, 5-6, 8-9, 12-19, and 21-23 as allegedly being obvious over Di Schiena (U.S. 4,866,067) in view of Weiner *et al.* To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

In order to establish a *prima facie* case of obviousness, the combined references must teach or suggest all of the claim limitations. MPEP § 2143.

Applicants have amended the claims to recite "consisting essentially of" in lieu of comprising." Again, the claims embody the specified materials "and those that do not materially affect the basic and novel characteristic(s)." More specifically, the claims do not recite oxyniacic acid, as the use of oxyniacic acid would materially alter the claimed composition. For example, Di Schiena states:

The acid component of salt (I), 3-carboxypyridine N-oxide, known also as, oxyniacic acid, is already employed in systemic therapy as lipemia-controlling drug, particularly the cholesterol and triglyceride fraction, and as vaso-activating agent, free from particular side-effects.

These very properties of oxyniacic acid allow to reasonably assume that the higher activity of the novel compound of formula (I), compared to Minoxidil alone is to be ascribed, as far as hair growth is concerned, to a *synergistic mechanism* whereby the lipidic component of the scalp, the altered composition of which is regarded as responsible for some forms of baldness, is favourably controlled and an effective micro-circulation, considered also very important for the optimum preservation of hair health, is restored.

From the foregoing it is clear that Di Schiena teaches that the combination of minoxidil and oxyniacic acid is *synergistic*. As such, the use of this particular acid would materially alter the claimed composition. The use of the "consisting essentially of" in the independent claims specifically excludes the use of oxyniacic acid as synergy is a material alteration. Further, the encapsulating technology of Weiner *et al.* has also been excluded as discussed above.

Applicants note that the differences between the claimed composition and Di Schiena no longer require the recitation of "homogeneous" nor the use of a specific water: ethanol ratio, to impart patentability. Di Schiena requires the use of the synergistic "oxyniacic acid" and the current claims specifically exclude features that materially affect the basic and novel characteristic(s). As such, the teaching of Di Schiena has been distinguished. Moreover, there is no motivation to combine Di Schiena with the acidification step of Weiner *et al.*, as Weiner *et al.* do not teach or suggest the use of the synergistic "oxyniacic acid." In view of the foregoing, the obviousness rejection has thus been overcome. Accordingly, the Examiner is respectfully requested to withdraw this rejection, and send this application to issue.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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